IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE CONTINUATION APPLICATION OF:
William J. Curatolo, et al. :

SERIAL NO.: To Be Assigned
(Continuation of Ser.No. 09/577,059) : EXAMINER:To Be Assigned

FILED: Herewith : ART UNIT: To Be Assigned

FOR: Controlled Release Dosage
Forms of Azithromycin

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Preliminary Amendment

In the matter of the continuation application filed herewith, please make the following changes to the application:

In the Specification:

Please insert the following sentence as the first paragraph in the specification, immediately following the title:

---This application is a continuation of copending U.S. Serial No. 09/577,059 (fully incorporated herein by reference), filed May 22, 2000, which is a division of U.S. Serial No. 08/727,634 (fully incorporated herein by reference), filed November 4, 1996, now U.S. Patent No. 6,068,859, issued May 30, 2000, which is a 371 of PCT/IB94/00264, filed April 13, 1995, which is a continuation-in-part of U.S. Serial No. 08/239,094, filed May 6, 1994, now abandoned.---

EXPRESS MAIL NO. EL 706320698US

In the claims:

Please add the following new claims 149-214, and then cancel claims 72-148.

149. A controlled release dosage form for oral administration to a human comprising a therapeutically effective amount of azithromycin and one or more additional components, said dosage form controlling a release rate of the azithromycin into the gastrointestinal tract of the human to which the dosage form is administered to decrease the incidence or severity of gastrointestinal side effects, said rate releasing the bulk of the azithromycin in a portion of the gastrointestinal tract distal to the duodenum.

150. The controlled release dosage form of claim 149 that releases 80% or more of the azithromycin in the portion of the gastrointestinal tract distal to the duodenum.

151. A controlled release dosage form for oral administration to a human comprising a therapeutically effective amount of azithromycin and one or more additional components, said dosage form controlling a release rate of the azithromycin into the gastrointestinal tract of the human to which the dosage form is administered to decrease the incidence or severity of gastrointestinal side effects, said rate releasing no more than 70% of the azithromycin within one-half hour from time of ingestion.

152. The dosage form of claim 150 that releases no more than about 10% of the azithromycin in the stomach.

153. The dosage form of claim 151 that releases no more than about 10% of the azithromycin in the stomach.

154. The dosage form of claim 153 wherein the azithromycin is in the form of a pharmaceutically acceptable salt.

155. The dosage form of claim 153 wherein the azithromycin is in an anhydrous form.

156. The dosage form of claim 153 wherein the azithromycin is in a hydrated form.

157. The dosage form of claim 156 wherein the azithromycin is in a dihydrate form.

158. The dosage form of claim 153 that releases no more than an additional 10% of the azithromycin during the first 30 minutes after the dosage form has exited the stomach.

159. The dosage form of claim 153 that releases no more than an additional 10% of the azithromycin during the first 15 minutes after the dosage form has exited the stomach.

160. The dosage form of claim 153 that releases no more than an additional 10% of the azithromycin during the first 15 minutes after the dosage form has entered the duodenum.

161. The dosage form of claim 153 wherein substantially all of the azithromycin is released for absorption in the gastrointestinal tract and before excretion from the body.

162. The dosage form of claim 153 wherein said azithromycin is present in an amount of from about 1 gram to about 7 grams.

163. The dosage form of claim 153 wherein said azithromycin is present in an amount of from about 1.5 grams to about 4 grams.

164. The dosage form of claim 150 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters.

165. The dosage form of claim 164 wherein said particles comprise azithromycin and a pharmaceutically acceptable carrier or diluent.

166. The dosage form of claim 151 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters.

167. The dosage form of claim 151 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 400 micrometers.

168. The dosage form of claim 152 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 400 micrometers.

169. The dosage form of claim 152 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters.

170. The dosage form of claim 149 comprising a plurality of particles, said particles having a diameter of less than about 350 micrometers.

171. The dosage form of claim 150 or claim 151 comprising a capsule, a tablet, a suspension or a sachet.

172. The dosage form of claim 164 comprising a sachet.

173. The dosage form of claim 164 wherein said particles further comprise a matrix material.

174. The dosage form of claim 173 wherein said matrix material is selected from the group consisting of waxes, cellulose and derivatives thereof, polymers; and mixtures thereof.

175. The dosage form of claim 174 further comprising a release-modifying agent.

176. The dosage form of claim 152 comprising a hydrogel.

177. The dosage form of claim 158, 159 or 160 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters, and said particles further comprising a core, said core having a first surface coating thereon.

178. The dosage form of claim 149, 150, or 151 comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters and said particles further comprising a core, said core having a first surface coating thereon.

179. The dosage form of claim 178 wherein said core comprises azithromycin and a pharmaceutically acceptable vehicle, carrier or diluent.

180. The dosage form of claim 177 wherein said first surface coating comprises a sustained release coating.

181. The dosage form of claim 177 wherein said first surface coating comprises a delayed release coating.

182. The dosage form of claim 178 wherein said first surface coating comprises a sustained release coating.

183. The dosage form of claim 177 wherein said first surface coating comprises a delayed release coating.

184. The dosage form of claim 177 further comprising a second surface coating on said core.

185. The dosage form of claim 178 further comprising a second surface coating on said core.

186. The dosage form of claim 184 wherein said second surface coating comprises a sustained release coating.

187. The dosage form of claim 185 wherein said second surface coating comprises a sustained release coating.

188. The dosage form of claim 184 wherein said second surface coating comprises an enteric coating.

189. The dosage form of claim 185 wherein said second surface coating comprises an enteric coating.

190. A controlled release multiparticulate dosage form of azithromycin comprising a plurality of particles, said particles having a diameter of from about 50 micrometers to about 3 millimeters and said particles further comprising a core, said core having one or more surface coating thereon.

191. A method for administering azithromycin to a human in need of treatment comprising orally administering a therapeutically effective amount of the dosage form of claim 150 or claim 151.

192. A method for administering azithromycin to a human in need of treatment comprising orally administering a therapeutically effective amount of the dosage form of claim 149.

193. A method of therapy comprising administering the dosage form of claim 159.

194. A method of therapy comprising administering the dosage form of claim 164 or claim 166.

195. The method of claim 194 comprising administering a single dose.

196. The method of claim 194 wherein the dosage form further comprises a multiparticulate form or a unit dose pack.

197. The method of claim 191 wherein the dosage form further comprises a bursting coated swelling core.

198. The method of claim 191 wherein the dosage form further comprises a membrane-moderated or reservoir system.

199. A method for administering azithromycin to a human in need of treatment comprising orally administering a therapeutically effective amount of the dosage form of claim 153.

200. The method of claim 199 wherein the dosage form further comprises a matrix multiparticulate.

201. A method for administering azithromycin to a human in need of treatment comprising orally administering a therapeutically effective amount of the dosage form of claim 158.

202. A method for administering azithromycin to a human in need of treatment comprising orally administering a therapeutically effective amount of the dosage form of claim 159.

203. The method of claim 201 wherein the dosage form comprises a delayed release dosage form.

204. The method of claim 203 wherein the delayed release dosage form is a pH-dependent coated tablet.

205. The method of claim 202 wherein the dosage form further comprises a bursting osmotic core device.

206. A method for preparing the dosage form of claim 150 comprising: granulating azithromycin bulk drug substance with a bind, and coating the resulting granules with one or more polymer coatings of controlled permeability to azithromycin, such that when administered to a human, said dosage form releases the bulk of the azithromycin in a portion of the gastrointestinal tract distal to the duodenum.

207. A method for preparing the dosage form of claim 151 comprising: granulating azithromycin bulk drug substance with a binder, and coating the resulting granules with one or more polymer coatings of controlled permeability to azithromycin, such that when administered to a human, said dosage form releases the bulk of the azithromycin in a portion of the gastrointestinal tract distal to the duodenum.

208. The dosage form of claim 149 comprising a matrix multiparticulate.

209. The dosage form of claim 151 comprising a matrix multiparticulate.

210. The dosage form of claim 208 wherein said matrix multiparticulate comprises a plurality of azithromycin-containing particles, each particle comprising a mixture of azithromycin with one or more excipients, said mixture forming the matrix limiting the release rate of the azithromycin into the gastrointestinal tract.

211. The dosage form of claim 209 wherein said matrix multiparticulate comprises a plurality of azithromycin-containing particles, each particle comprising a mixture of azithromycin with one or more excipients, said mixture forming the matrix limiting the release rate of the azithromycin into the gastrointestinal tract.

212. The dosage form of claim 208 wherein said release rate is such that no more than 70% of the azithromycin is released within about one-half hour from time of ingestion.

213. A method for reducing the incidence and severity of azithromycin gastrointestinal side effects in a human orally dosed with a therapeutically effective amount of azithromycin comprising limiting the exposure of the duodenum to orally dosed azithromycin.

214. A method for reducing the incidence and severity of azithromycin gastrointestinal side effects in a human orally dosed with a therapeutically effective amount of azithromycin comprising increasing the ileocecal absorption of azithromycin and decreasing the duodenal absorption of azithromycin in the gastrointestinal tract of the human.

REMARKS

New claims 149-214 have been added. Of these new claims, claims 149,151,190, 213 and 214 are independent. Support for the new claims can be found *inter alia* at the following portions of the instant specification: page 2, lines 10-24; pages 69-75, and pages 46-50.

Authorization is hereby given to charge any fees to Deposit Account No. 16-1445.

Applicants provide herewith an Associate Power of Attorney.

Action on the merits, especially a Notice of Allowance, is respectfully requested.

Respectfully submitted,

DATE: 3/9/01

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